

### REMARKS

Reconsideration and allowance are respectfully requested.

Claims 6-11, 13, 16-18 and 25-34 are pending. The amendments are supported by the original disclosure and, thus, no new matter is added by their entry. The claims are limited to administration of human protein S. Entry of the amendment is requested because it simply incorporates the limitation of a dependent claims (i.e., "wherein the protein S polypeptide is human protein S") and it would reduce the issues on appeal. Applicant do so to facilitate prosecution in this application and maintain that variants are within the scope of their invention. Thus, the present amendments are made without prejudice to prosecuting the broader subject matter in the future.

### *35 U.S.C. 112 – Enablement*

The Patent Office has the initial burden to question the enablement provided for the claimed invention. M.P.E.P. § 2164.04, and the cases cited therein. It is incumbent upon the Patent Office, whenever a rejection on this basis is made, to explain why it doubts the truth or accuracy of any statement in a supporting disclosure and to back up assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement. *In re Marzocchi*, 169 USPQ 367, 370 (C.C.P.A. 1971). Specific technical reasons are always required. See M.P.E.P. § 2164.04.

Claims 6, 8-11, 13, 16-18, 25, 27-30 and 32-34 were rejected under Section 112, first paragraph, because the specification allegedly "does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims." Applicants traverse because requiring the administration of human protein S in claims 6, 25 and 30 – which the Examiner admits is enabled by the present specification – moots this rejection. Further, the present amendment incorporates the limitation of claims 7, 26 and 31 (i.e., "wherein the protein S polypeptide is human protein S") into the independent claims from which they depend. Claims 7, 26 and 31 were not rejected in the Office Action. Therefore, the present claims are clearly enabled.

Withdrawal of the enablement rejection is requested because it would not require undue experimentation for a person of skill in the art to make and use the invention.

### *35 U.S.C. 112 – Written Description*

The specification must convey with reasonable clarity to persons skilled in the art that applicant was in possession of the claimed invention as of the filing date sought. See *Vas-Cath v. Mahurkar*, 19 USPQ2d 1111, 1117 (Fed. Cir. 1991). But the Patent Office has the initial burden of presenting evidence or a reason why persons of ordinary skill in the art would not have recognized such a description of the claimed invention in the original disclosure. See *In re Gosteli*, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989).

Claims 6, 8-11, 13, 16-18, 25, 27-30 and 32-34 were rejected under Section 112, first paragraph, because they allegedly contain “subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.” Applicants traverse because requiring the administration of human protein S into claims 6, 25 and 30 Applicants traverse because limiting the claims 6, 25 and 30 to administering human protein S – which is described by the present specification – moots this rejection. Further, the present amendment incorporates the limitation of claims 7, 26 and 31 (i.e., “wherein the protein S polypeptide is human protein S”) into the independent claims from which they depend. Claims 7, 26 and 31 were not rejected in the Office Action. Therefore, the present claims are clearly described.

Withdrawal of the written description rejection is requested because the specification conveys to a person skilled in the art that Applicants were in possession of the claimed invention as of the filing date.

### *35 U.S.C. 112 – Definiteness*

Claims 6, 8-11, 13, 16-18, 25, 27-30 and 32-34 were rejected under Section 112, second paragraph, as allegedly indefinite. Applicants traverse because the present amendments delete reference to sequences less than 100% identical to human protein S. Thus the Examiner's objection is moot.

Applicants request withdrawal of the Section 112, second paragraph, rejection because the pending claims are clear and definite.

*35 U.S.C. 102 – Novelty*

A claim is anticipated only if each and every limitation as set forth in the claim is found, either expressly or inherently described, in a single prior art reference. *Verdegaal Bros. v. Union Oil Co. of Calif.*, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). The identical invention must be shown in as complete detail as is claimed. See *Richardson v. Suzuki Motor Co.*, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989).

Claims 6-11, 13 and 16-18 were rejected as allegedly anticipated by Bouma et al. (U.S. Patent 5,663,142). Applicants traverse because their claims require administration to a human subject of human protein S in the absence of protein C and activated protein C (APC). Bouma fails to teach any administration of an effective amount of polypeptide. Only in vitro assays of protein S activity are performed. No administration to a human subject is disclosed. No human protein S is administered. Bouma is concerned only with the use of mutant protein S. Instead of teaching administration of human protein S in the absence of protein C and APC, the paragraph bridging cols. 11-12 specifically contemplates their co-administration with the mutant protein S. Therefore, Bouma does not disclose each and every limitation as set forth in the claim.

Claims 6, 8-11, 13, 16-18, 25, 27-30 and 32-34 were rejected as allegedly anticipated by Bertilsson (U.S. Appln. 2003/0165485). Applicants traverse because the limitation of claims 7, 26 and 31 is incorporated in the independent claims. The present claims require administration of human protein S. The Examiner did not allege that the cited document teaches Applicants' claimed invention since claims 7, 26 and 31 were excluded from this rejection. Therefore, Bertilsson does not disclose each and every limitation as set forth in the claim.

Withdrawal of the Section 102 rejections is requested because the cited prior art documents fail to disclose all limitations of the claimed invention.

35 U.S.C. 103 – *Nonobviousness*

A claimed invention is unpatentable if the differences between it and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art. *In re Kahn*, 78 USPQ2d 1329, 1334 (Fed. Cir. 2006) citing *Graham v. John Deere*, 148 USPQ 459 (1966). The *Graham* analysis needs to be made explicitly. *KSR v. Teleflex*, 82 USPQ2d 1385, 1396 (2007). It requires findings of fact and a rational basis for combining the prior art disclosures to produce the claimed invention. See *id.* (“Often, it will be necessary for a court to look to interrelated teachings of multiple patents . . . and the background knowledge possessed by a person having ordinary skill in the art, all in order to determine whether there was an apparent reason to combine the known elements in the fashion claimed by the patent at issue”). The use of hindsight reasoning is impermissible. See *id.* at 1397 (“A factfinder should be aware, of course, of the distortion caused by hindsight bias and must be cautious of arguments reliant upon *ex post* reasoning”). Thus, a *prima facie* case of obviousness requires “some rationale, articulation, or reasoned basis to explain why the conclusion of obviousness is correct.” *Kahn* at 1335; see *KSR* at 1396. A claim directed to a combination of prior art elements “is not proved obvious merely by demonstrating that each of its elements was, independently, known in the prior art.” *Id.* Finally, a determination of *prima facie* obviousness requires a reasonable expectation of success. See *In re Rinehart*, 189 USPQ 143, 148 (C.C.P.A. 1976).

Claims 6-11, 13 and 16-18 were rejected as allegedly unpatentable over Hung (U.S. Appln. 2003/0060415). Applicants traverse because Hung is concerned with treatment of coronary and cardiovascular conditions. There is no reasonable expectation that administration to a human subject of human protein S provides “neuroprotection after brain injury caused by at least cerebral ischemia, hypoxia, re-oxygenation, or a combination thereof” as required by Applicants’ claims. Further, there is no reasonable expectation that neuroprotection would be achieved without also administration of protein C or activated protein C (APC). Hung fails to explicitly teach or suggest that no protein C or APC is administered, there is no deficiency of protein S activity in the

human subject, or that any of the recited results of treatment were achieved. Therefore, the present claims are not obvious over Hung.

Claims 6-11, 13, 16-18 and 25-34 were rejected as allegedly unpatentable over Bertilsson in view of Hung. Applicants traverse because the deficiencies of Bertilsson and Hung discussed above are not remedied by their combination. The cited documents alone or in combination fail to teach or suggest any beneficial effect of human protein S on neuroprotection. In Bertilsson, the beneficial effect of protein S is on the neural stem cell and neural progenitor cell. And Hung is concerned with treatment of coronary and cardiovascular conditions. The cited document contain no teaching or suggestion of an effect on neuroprotection as required by Applicants' claims. There is also no reasonable expectation that administration to a human subject of human protein S provides "neuroprotection after brain injury caused by at least cerebral ischemia, hypoxia, re-oxygenation, or a combination thereof" as required by Applicants' claims. Further, there is no reasonable expectation that neuroprotection would be achieved without also administration of protein C or activated protein C (APC).

Withdrawal of the Section 103 rejections is requested because the claims would not have been obvious to one of ordinary skill in the art when this invention was made.

#### *Conclusion*

Having fully responded to the pending Office Action, Applicants submit that the claims are in condition for allowance and earnestly solicit an early Notice to that effect. The Examiner is invited to contact the undersigned if any further information is required.

Respectfully submitted,

**NIXON & VANDERHYE P.C.**

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